1: Curr Biol. 1996 Dec 1;6(12):1669-76. Related Articles, Links

Apo-3, a new member of the tumor necrosis factor receptor family, contains a death domain and activates apoptosis and NF-kappa B.

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BACKGROUND: Two receptors that contain the so-called "death domain' have been described to date: tumor necrosis factor receptor 1 (TNFR1) and Fas/Apo-1 (CD95); both belong to the TNFR gene family. The death domain of TNFR1 mediates the activation of programmed cell death (apoptosis) and of the transcription factor NF-kappa B, whereas the death domain of CD95 only appears to activate apoptosis. RESULTS: We have identified an additional member of the TNFR family, which we have named Apo-3. Apo-3 is a transmembrane protein of approximately 47 kDa that has similarity of members of the TNFR family in its extracellular, cysteine-rich domains. In addition, Apo-3 resembles TNFR1 and CD95 in that it contains a cytoplasmic death domain. The Apo-3 gene mapped to human chromosome 1p36.3, and Apo-3 mRNA was detected in several human tissues, including spleen, thymus, peripheral blood lymphocytes, small intestine and colon. Ectopic expression of Apo-3 in HEK293 or HeLa cells induced marked apoptosis. CrmA, a poxvirus inhibitor of Ced-3-like proteases which blocks death signaling by TNFR1 and CD95, inhibited Apo-3-induced apoptosis. Ectopic expression of Apo-3 also induced the activation of NF-kappa B. Apo-3 did not specifically bind to the Apo-2 ligand, suggesting the existence of a distinct ligand for Apo-3. CONCLUSIONS: These results identify Apo-3 as a third member of the TNFR family that activates apoptosis, and suggest that Apo-3, TNFR1 and CD95 engage a common apoptotic cell-death machinery. Apo-3 resembles TNFR1 because it can stimulate NF-kappa B activity and regulate apoptosis. Apo-3 mRNA is expressed in various tissues, consistent with the possibility that this receptor may regulate multiple signaling functions.

1: Curr Biol. 1997 Dec 1;7(12):1003-6.

A novel receptor for Apo2L/TRAIL contains a truncated death domain.

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Apo2 ligand (Apo2L [1], also called TRAIL for tumor necrosis factor (TNF)-related apoptosis-inducing ligand [2]) belongs to the TNF family and activates apoptosis in tumor cells. Three closely related receptors bind Apo2L: DR4 and DR5, which contain cytoplasmic death domains and signal apoptosis, and DcR1, a decoy receptor that lacks a cytoplasmic tail and inhibits Apo2L function [3-5]. By cross-hybridization with DcR1, we have identified a fourth Apo2L receptor, which contains a cytoplasmic region with a truncated death domain. We subsequently named this protein decoy receptor 2 (DcR2). The DcR2 gene mapped to human chromosome 8p21, as did the genes encoding DR4, DR5 and DcR1. A single DcR2 mRNA transcript showed a unique expression pattern in human tissues and was particularly abundant in fetal liver and adult testis. Upon overexpression, DcR2 did not activate apoptosis or nuclear factor-kappaB; however, it substantially reduced cellular sensitivity to Apo2L-induced apoptosis. These results suggest that DcR2 functions as an inhibitory Apo2L receptor.

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